



Sheet 1 of 9

FORM PTO-1449
(REV. 7-80)U.S. DEPARTMENT OF COMMERCE
PATENT AND TRADEMARK OFFICEATTY. DOCKET NO.
660088.438APPLICATION NO.
09/765,104

INFORMATION DISCLOSURE STATEMENT

(Use several sheets if necessary)

APPLICANTS

Anne N. Murphy and Amy K. Stout

FILING DATE

January 16, 2001

GROUP ART UNIT

1645

U.S. PATENT DOCUMENTS

*EXAMINER INITIAL		DOCUMENT NUMBER	DATE	NAME	CLASS	SUBCLASS	FILING DATE IF APPROPRIATE
JS	AA	5,049,673	09/17/91	Tsien et al.	546	107	
	AB	5,459,251	10/17/95	Tsujimoto et al.	536	23.5	
	AC	5,501,980	03/26/96	Katerinopoulos et al.	436	74	
JS	AD	5,888,498	03/30/99	Davis et al.	424	93.21	

FOREIGN PATENT DOCUMENTS

		DOCUMENT NUMBER	DATE	COUNTRY	TRANSLATION	
					YES	NO
	AE					

OTHER PRIOR ART (Including Author, Title, Date, Pertinent Pages, Etc.)

JS	AF	Aizu et al., "Anthralin, A Non-TPA Type Tumor Promoter, Synergistically Enhances Phorbol Ester-Caused Prostaglandin E ₂ Release From Primary Cultured Mouse Epidermal Cells," <i>Japan. J. Pharmacol.</i> 60(1):9-17, September 1992.
	AG	Antoniou et al., "Inhibitors Of Ca ²⁺ Release From The Isolated Sarcoplasmic Reticulum. I. Ca ²⁺ Channel Blockers," <i>Biochem. Biophys. Acta</i> 816(1):9-17, June 11, 1985.
	AH	Ashkenazi et al., "Death Receptors: Signaling and Modulation," <i>Science</i> 281(5381):1305-1308, August 28, 1998.
	AI	Badaoui et al., "Effects of Cyclopiazonic Acid on Membrane Currents, Contraction and Intracellular Calcium Transients in Frog Heart," <i>J. Mol. Cell. Cardiol.</i> 27(11):2495-2505, November 1995.
	AJ	Begum et al., "Stimulation of Protein Phosphatase-1 Activity by Insulin in Rat Adipocytes. Evaluation of the role of mitogen-activated protein kinase pathway," <i>J. Biol. Chem.</i> 270(2):709-714, January 13, 1995.
	AK	Bernardi et al., "Modulation of the Mitochondrial Cyclosporin A-Sensitive Permeability Transition Pore. I. Evidence for two separate Me ²⁺ binding sites with opposing effects on the pore open probability," <i>J. Biol. Chem.</i> 268(2):1005-1010, January 15, 1993.
	AL	Bernardi et al., "Modulation of the Mitochondrial Permeability Transition Pore. Effect of Protons and Divalent Cations," <i>J. Biol. Chem.</i> 267(5):2934-2939, February 15, 1992.
JS	AM	Berridge et al., "Cytosolic calcium oscillators," <i>FASEB J.</i> 2(15):3074-3082, December 1988.

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Jeffrey Seiw

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BB			

OTHER PRIOR ART (Including Author, Title, Date, Pertinent Pages, Etc.)

JS	BC	Beutner et al., "Complexes Between Porin, Hexokinase, Mitochondrial Creatine Kinase and Adenylate Translocator Display Properties of the Permeability Transition Pore, Implication for Regulation of Permeability Transition by the Kinases," <i>Biochim. Biophys. Acta</i> 1368:7-18, 1998.
	BD	Brini et al., "A Calcium Signaling Defect in the Pathogenesis of a Mitochondrial DNA Inherited Oxidative Phosphorylation Deficiency," <i>Nature Medicine</i> 5(8):951-954, August 1999.
	BE	Budd et al., "A Reevaluation of the Role of Mitochondria in Neuronal Ca ²⁺ Homeostasis," <i>J. Neurochemistry</i> 66(1):403-411, January 1996.
	BF	Chen et al., "Molecular Identification of the Ryanodine Receptor Ca ²⁺ Sensor," <i>J. Biol. Chem.</i> 273(24):14675-14678, June 12, 1998.
	BG	Chiesi et al., "Inhibition of Rapid Ca-Release from Isolated Skeletal and Cardiac Sarcoplasmic Reticulum (SR) Membranes," <i>Biochemical and Biophysical Research Communications</i> 154(1):1-8, July 15, 1988.
	BH	Crompton et al., "On the Involvement of a Mitochondrial Pore in Reperfusion Injury," <i>Basic Research in Cardiology</i> 88(5): 513-523, September-October 1993.
	BI	Darley-USmar et al., "Mitochondria, Oxygen and Reperfusion Damage," <i>Annals of Medicine</i> 23:583-588, 1991.
JS	BJ	Dyken, "Free Radicals and Mitochondrial Dysfunction in Excitotoxicity and Neurodegenerative Disease" in V. E. Koliatos and R.R. Ratan, eds., <i>Cell Death and Diseases of the Nervous System</i> , Humana Press, New Jersey, 1999, pages 45-68.

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CB			

OTHER PRIOR ART (Including Author, Title, Date, Pertinent Pages, Etc.)

JS	CC	Dykens, "Isolated Cerebral and Cerebellar Mitochondria Produce Free Radicals when Exposed to Elevated CA^{2+} and Na^{+} : Implications for Neurodegeneration," <i>J. Neurochemistry</i> 63(2):584-591, August 1994.
	CD	Dykens, "Mitochondrial Radical Production and Mechanisms of Oxidative Excitotoxicity" in K.J.A. Davies, and F. Ursini, eds., <i>The Oxygen Paradox</i> , Cleup Press, U. of Padova, 1995, pages 453-467.
	CE	Dykens, <i>Mitochondria and Free Radicals in Neurodegenerative Diseases</i> , Beal, Howell and Bodis-Wollner, Eds., Wiley-Liss Inc., New York, 1997, Chapter 3, "Mitochondrial Free Radical Production and Oxidative Pathophysiology: Implications for Neurodegenerative Disease," pp. 29-55.
	CF	Ellerby et al., "Establishment of a Cell-Free System of Neuronal Apoptosis: Comparison of Premitochondrial, Mitochondrial, and Postmitochondrial Phases," <i>J. Neuroscience</i> 17(16):6165-6178, August 15, 1997.
	CG	Emerson et al., "The Component of 'Ruthenium Red' Responsible for Inhibition of Mitochondrial Calcium Ion Transport. Spectra, Electrochemistry, and Aquation Kinetics. Crystal Structure of μ -O-[(HCO ₂)(NH ₃) ₄ Ru] ₂ Cl ₃ ," <i>J. Amer. Chem. Soc.</i> 115:11799-11805, 1993.
	CH	Ernster et al., "Mitochondria: A Historical Review," <i>J. of Cell Biology</i> 91(3Pt.2):227s-255s, December 1981.
	CI	Fiskum et al., "The Cytoskeleton of Digitonin-Treated Rat Hepatocytes," <i>Proc. Nat. Acad. Sci. USA</i> 77(6):3430-3434, June 1980.
JS	CJ	Green et al., "Mitochondria and Apoptosis," <i>Science</i> 281:1309-1312, August 28, 1998.

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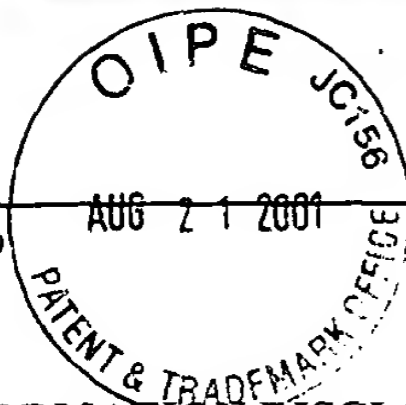
Jeffrey S. Smith

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JS	DC	Green, "Apoptotic Pathways: The Roads to Ruin," <i>Cell</i> 94:695-698, September 18, 1998.
	DD	Guerini, "Calcineurin: Not Just a Simple Protein Phosphatase," <i>Biochem. Biophys. Res. Commun.</i> 235:271-275, 1997.
	DE	Gunter and Gunter, "Transport of Calcium by Mitochondria," <i>J. Bioenergetics and Biomembranes</i> 26(5): 471-485, 1994.
	DF	Gunter et al., "The Ca ²⁺ Transport Mechanisms of Mitochondria and Ca ²⁺ Uptake From Physiological-Type Ca ²⁺ Transients," <i>Biochim. Biophys. Acta</i> 1366:5-15, 1998.
	DG	Gunter et al., "Mechanisms by Which Mitochondria Transport Calcium," <i>Am. J. Physiol.</i> 258 (Cell Physiol. 27): C755-C786, May 1990.
	DH	Gunter et al., "Mitochondrial Calcium Transport: Physiological and Pathological Relevance," <i>Am. J. Physiol.</i> 267(Cell Physiol. 36):C313-C339, August 1994.
	DI	Hatanaka et al., "A Role of Peroxides in Ca ²⁺ Ionophore-Induced Apoptosis in Cultured Rat Cortical Neurons," <i>Biochem. Biophys. Res. Commun.</i> 227(2):513-518, October 14, 1996.
	DJ	Hepworth et al., "Okadaic Acid Induces the Release of Ca ²⁺ from Intracellular Stores in ECV304 Endothelial Cells," <i>Cell Calcium</i> 21(6):461-467, June 1997.
	DK	Heytler, "Uncouplers of Oxidative Phosphorylation," <i>Pharmacol. Ther.</i> 10(3):461-472, 1980.
	DL	Heytler, "Uncouplers of Oxidative Phosphorylation," <i>Methods of Enzymology</i> 55:462-472, 1979.
	DM	Hockerman et al., "Molecular Determinants of Drug Binding and Action on L-Type Calcium Channels," <i>Annu. Rev. Pharmacol. Toxicol.</i> 37:361-396, 1997.
	DN	Hurley, "Kinetics of High-Affinity Ca ²⁺ Sequestration in Permeabilized Rat Pancreatic Acini," <i>Am. J. Physiol.</i> 254(Cell Physiol. 23):C621-C627, May 1988.
	DO	Ikura, "Calcium Binding and Conformational Response in EF-Hand Proteins," <i>TIBS</i> 21:14-17, January 1996.
JS	DP	Jan and Jan, "Tracing the Roots of Ion Channels," <i>Cell</i> 69:715-718, May 29, 1992.

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EB				

OTHER PRIOR ART (Including Author, Title, Date, Pertinent Pages, Etc.)

JS	EC	Jürgensmeier et al., "Bax Directly Induces Release of Cytochrome c from Isolated Mitochondria," <i>Proc. Nat. Acad. Sci. USA</i> 95:4997-5002, April 1998.
	ED	Jurkowitz-Alexander et al., "Cell Swelling, Blebbing, and Death Are Dependent on ATP Depletion and Independent of Calcium During Chemical Hypoxia in a Glial Cell Line (ROC-1)," <i>J. Neurochemistry</i> 59:344352, 1992.
	EE	Kakalis et al., "Characterization of the Calcium-Binding Sites of Calcineurin B," <i>FEBS Letters</i> 362:55-58, 1995.
	EF	Kapùs et al., "Is the Mitochondrial Ca ²⁺ Uniporter a Voltage-Modulated Transport Pathway?," <i>FEBS Lett.</i> 282(1):61-64, April 22, 1991.
	EG	Kroemer et al., "The Mitochondrial Death/Life Regulator in Apoptosis and Necrosis," <i>Annu. Rev. Physiol.</i> 60:619-642, 1998.
	EH	Kroemer, "The Proto-Oncogene Bcl-2 and Its Role in Regulating Apoptosis," <i>Nature Medicine</i> 3(6):614-620, June 1997.
	EI	Leist and Nicotera, "Calcium and Neuronal Death," <i>Rev. Physiol. Biochem. Pharmacol.</i> 132:79, 1998.
	EJ	Levy et al., "Alkali Cation Transport Through Liposomes by the Antimicrobial Fusafungine and its Constitutive Enniatins," <i>Biochem. Pharmacol.</i> 50(12):2105-2107, December 22, 1995.
	EK	Li et al., "Amelioration by Cyclosporin A of Brain Damage Following 5 or 10 min of Ischemia in Rats Subjected to Preischemic Hyperglycemia," <i>Brain Research</i> 753(1):133-140, April 4, 1997.
	EL	Liu et al., "Induction of Apoptotic Program in Cell-Free Extracts: Requirement for dATP and Cytochrome c," <i>Cell</i> 86:147-157, July 12, 1996.
JS	EM	Low et al., "Effects of Thapsigargin and Ryanodine on Vascular Contractility: Cross-talk Between Sarcoplasmic Reticulum and Plasmalemma," <i>Eur. J. Pharmacol.</i> 230(1):53-62, January 5, 1993.

EXAMINER

Jeffrey Biew

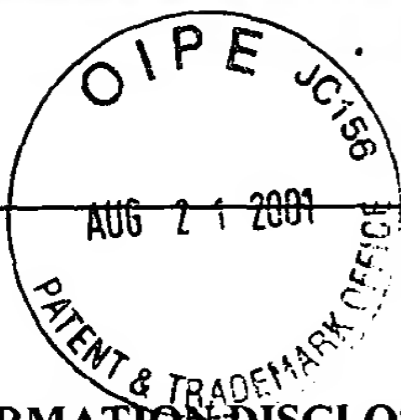
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FA						

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FB			

OTHER PRIOR ART (Including Author, Title, Date, Pertinent Pages, Etc.)

JS	FC	Matlib et al., "Oxygen-Bridged Dinuclear Ruthenium Amine Complex Specifically Inhibits Ca ²⁺ Uptake into Mitochondria <i>In Vitro</i> and <i>In Situ</i> in Single Cardiac Myocytes," <i>J. Biol. Chem.</i> 273(17):10223-10231, April 24, 1998.
	FD	McCormack et al., "Studies on Mitochondrial Ca ²⁺ -Transport and Matrix Ca ²⁺ Using Fura-2-Loaded Rat Heart Mitochondria," <i>Biochim. Biophys. Acta</i> 973:420-427, 1989.
	FE	Møller et al., "Charge Screening by Cations Affects the Conformation of the Mitochondrial Inner Membrane. A Study of Exogenous MAD(P)H Oxidation in Plant Mitochondria," <i>Biochem. J</i> 195(3):583-588, June 1, 1981.
	FF	Murphy et al., "Bcl-2 Potentiates the Maximal Calcium Uptake Capacity of Neural Cell Mitochondria," <i>Proc. Natl. Acad. Sci. USA</i> 93:9893-9898, September 1996.
	FG	Murphy et al., <i>Mitochondria and Free Radicals in Neurodegenerative Diseases</i> , Beal, Howell and Bodis-Wollner, Eds., Wiley-Liss, New York, 1998, Chapter 8, "Mitochondria, Reactive Oxygen Species, and Apoptosis," pp. 159-186.
	FH	Muscari et al., "Mitochondrial Function and Superoxide Generation from Submitochondrial Particles of Aged Rat Hearts," <i>Biochim. Biophys. Acta</i> 1015(2):200-204, February 2, 1990.
	FI	Newmeyer et al., "Cell-Free Apoptosis in Xenopus Egg Extracts: Inhibition by Bcl-2 and Requirement for an Organelle Fraction Enriched in Mitochondria," <i>Cell</i> 79:353-364, October 12, 1994.
	FJ	Obatomi and Bach, "Inhibition of Mitochondrial Respiration and Oxygen Uptake in Isolated Rat Renal Tubular Fragments by Atractyloside," <i>Toxicol. Lett.</i> 89:155-161, 1996.
	FK	Orrenius and Nicotera, "The Calcium Ion and Cell Death," <i>J. Neural. Transm.</i> 43[Suppl.]:1-11, 1994.
JS	FL	Persechini et al., "The EF-Hand Family of Calcium-Modulated Proteins," <i>TINS</i> 12(11):462-467, 1989.

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					YES	NO
	GB					

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JS	GC	Petronilli et al., "Transient and Long-Lasting Openings of the Mitochondrial Permeability Transition Pore Can Be Monitored Directly in Intact Cells by Changes in Mitochondrial Calcein Fluorescence," <i>Biophysical Journal</i> 76:725-734, February 1999.
	GD	Radi et al., <i>Mitochondria and Free Radicals in Neurodegenerative Diseases</i> , Beal, Howell and Bodis-Wollner, Eds., Wiley-Liss, New York, 1998, Chapter 4, "Free Radical Damage to Mitochondria," pp. 57-89.
	GE	Raff, "Cell Suicide for Beginners," <i>Nature</i> 396(6707):119-122, November 12, 1998.
	GF	Reed et al., "The Inhibition of Mitochondrial Calcium Transport by Lanthanides and Ruthenium Red," <i>Biochem. J.</i> 140(2):143-155, May 1974.
	GG	Ridgley et al., "Reactive Oxygen Species Activate a Ca^{2+} -Dependent Cell Death Pathway in the Unicellular Organism <i>Trypanosoma brucei brucei</i> ," <i>Biochem. J.</i> 340:33-40, 1999.
	GH	Rottenberg et al., "Regulation of Ca^{2+} Transport in Brain Mitochondria. II. The Mechanism of the Adenine Nucleotides Enhancement of Ca^{2+} Uptake and Retention," <i>Biochim. Biophys. Acta</i> 1016(1):87-98, March 15, 1990.
	GI	Salvador et al., "Characterization of the Intracellular and the Plasma Membrane Ca^{2+} -ATPases in Fractionated Pig Brain Membranes Using Calcium Pump Inhibitors," <i>Arch. Biochem. Biophys.</i> 351(2):272-278, March 15, 1998.
	GJ	Sastrasinh et al., "Glutamine Transport in Submitochondrial Particles," <i>Am. J. Physiol.</i> 257(Renal Fluid Electrolyte Physiol. 26):F1050-F1058, December 1989.
JS	GK	Scorrano et al., "Chloromethyltetramethylrosamine (Mitotracker Orange TM) Induces the Mitochondrial Permeability Transition and Inhibits Respiratory Complex I. Implications for the Mechanism of Cytochrome <i>c</i> Release," <i>J. Biol. Chem.</i> 274(35):24567-24663, August 27, 1999.

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JS	HC	Srivastava et al., "Atovaquone, a Broad Spectrum Antiparasitic Drug, Collapses Mitochondrial Membrane Potential in a Malarial Parasite," <i>J. Biol. Chem.</i> 272(7):3961-3966, February 14, 1997.
	HD	Stout et al., "Glutamate-Induced Neuron Death Requires Mitochondrial Calcium Uptake," <i>Nature Neuroscience</i> 1(5):366-373, September 1998.
	HE	Streb et al., "Release of Ca ²⁺ from a Nonmitochondrial Intracellular Store in Pancreatic Acinar Cells by Inositol-1,4,5-Trisphosphate," <i>Nature</i> 306(5938):67-69, November 3-9, 1983.
	HF	Susin et al., "Mitochondria as Regulators of Apoptosis: Doubt No More," <i>Biochimica et Biophysica Acta</i> 1366:151-165, 1998.
	HG	Szabó et al., "Modulation of the Mitochondrial Megachannel by Divalent Cations and Protons," <i>J. Biol. Chem.</i> 267(5):2940-2946, February 15, 1992.
	HH	Takei et al., "Ca ²⁺ Ionophore-Induced Apoptosis on Cultured Embryonic Rat Cortical Neurons," <i>Brain Research</i> 652(1):65-70, 1994.
	HI	Takemura et al., "Activation of Calcium Entry by the Tumor Promoter Thapsigargin in Parotid Acinar Cells. Evidence that an Intracellular Calcium Pool and not an Inositol Phosphate Regulates Calcium Fluxes at the Plasma Membrane," <i>J. Biol. Chem.</i> 264(21):12266-12271, July 25, 1989.
	HJ	Tencé et al., "Synergistic Effects of Acetylcholine and Glutamate on the Release of Arachidonic Acid from Cultured Striatal Neurons," <i>J. Neurochem.</i> 64(4):1605-1613, April 1995.
	HK	Thastrup et al., "Thapsigargin, a Novel Molecular Probe for Studying Intracellular Calcium Release and Storage," <i>Agents Actions</i> 27(1/2):17-23, April 1989.
JS	HK	Tong et al., "Synaptic Desensitization of NMDA Receptors by Calcineurin," <i>Science</i> 267:1510-1512, March 10, 1995.

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JS	II		White and Reynolds, "Mitochondrial Depolarization in Glutamate-Stimulated Neurons: An Early Signal Specific to Excitotoxin Exposure," <i>J. of Neuroscience</i> 16(18):5688-5697, September 15, 1996.
	IJ		Williams et al., "Structure and Functional Expression of an ω -Conotoxin-Sensitive Human N-Type Calcium Channel," <i>Science</i> 257:389-395, July 17, 1992.
	IK		Won et al., "Role of Inositol Trisphosphate-Sensitive Calcium Stores in the Regulation of Adrenocorticotropin Secretion by Perifused Rat Anterior Pituitary Cells," <i>Endocrinology</i> 136(12):5399-5408, December 1995.
	IL		Xie et al., "Structure of the Regulatory Domain of Scallop Myosin at 2.8 Å Resolution," <i>Nature</i> 368:306-312, March 24, 1994.
	IM		Yan et al., "Activation of Muscarinic Cholinergic Receptors Blocks Apoptosis of Cultured Cerebellar Granule Neurons," <i>Molecular Pharmacology</i> 47(2):248-257, February 1995.
	IN		Ying et al., "Inhibition of Mitochondrial Calcium Ion Transport by an Oxo-Bridged Dinuclear Ruthenium Ammine Complex," <i>Biochemistry</i> 30(20):4949-4952, May 21 1991
JS	IO		Zoratti and Szabò, "The Mitochondrial Permeability Transition," <i>Biochimica et Biophysica Acta</i> 1241:139-176, 1995.

EXAMINER

Jeffrey Seew

DATE CONSIDERED

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* EXAMINER: Initial if reference considered, whether or not criteria is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant(s).

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